PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

GILSON et al.

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For: EMBOLIC PROTECTION DEVICE

DECLARATION OF DR. GARY ROUBIN

Commissioner for Patents
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I, Dr. Gary Roubin, do declare and state as follows:

1. I am a medical doctor, with an M.D. from the University of Queensland, and have been an interventional cardiologist since 1984.
2. I am currently a clinical Professor of Medicine at New York University School of Medicine.
3. From 1997 to 2003, and during the events discussed below, I was Chief of Endovascular Services at Lenox Hill Hospital in New York, New York, USA.
4. I am familiar with angioplasty procedures and with interventional devices used in such procedures, and have performed approximately 2000 carotid artery angioplasty/stent procedures.
5. In February, March, and April, 1998, I worked with Paul Gilson of MedNova, and conducted tests of MedNova's prototype "NeuroShield" embolic filter protection devices, to determine if the devices were practically useful for filtering emboli out of blood flowing through a blood vessel, such as a carotid artery.

6. When a carotid artery becomes partially blocked by a stenosis, it is necessary to restore blood flow to the brain, either by surgically removing the stenosis, or by an angioplasty procedure involving balloon catheter dilation of the stenosis, followed by implanting a stent at the site of the lesion. During the procedure of dilating the stenosis and expanding a stent in the vessel, small pieces of the plaque called emboli may be released into the bloodstream. Such emboli are potentially lethal, because they may obstruct blood vessels in the brain, causing a stroke. Although there are many advantages to treating carotid artery blockages by angioplasty, an embolic filter capable of filtering blood flowing through the vessel, and removing emboli released from the stenosis, is essential to this treatment.

7. In order to perform carotid artery angioplasty, it is necessary for an operator to insert a primary guidewire into the femoral artery, and to thread the guidewire through the vascular system to reach the carotid artery in the neck. A guide catheter is then inserted over the primary guidewire to a position that is proximal of the carotid artery lesion to be treated, and the primary guidewire is removed. An embolic filter is compressed into a delivery catheter, and the delivery catheter is inserted through the guide catheter to a position distal of the lesion.

8. In order to insert the delivery catheter and filter to a position distal of the lesion, it is necessary to guide the delivery catheter through the stenosis, using a guidewire that extends through and beyond the distal end of the filter. It is essential to be able to maneuver the guidewire on which the filter is disposed through the lesion, prior to deploying the filter in the vessel. When the filter is deployed in the vessel, in a position distal of the lesion, it is important that the filter be maintained in position during subsequent manipulation of the guidewire, in order to maintain contact of the filter with the vessel walls and prevent emboli from escaping past the filter. For this reason, it is desirable that an operator be able to rotate or

distally translate the guidewire relative to the filter element without displacing the expanded filter element deployed in the vessel.

9. In performing angioplasty procedures, treatment devices such as balloon catheters and stent delivery catheters are advanced along the guidewire to a position proximal of the filter element. It is equally important that these treatment procedures should not displace the filter element during treatment.

10. Because the carotid arteries supply blood to the brain, any occlusion of the carotid arteries during treatment such as angioplasty can have serious or fatal consequences. In order to determine whether a medical device such as an embolic filter is effective to remove emboli, and safe enough for human use, it is possible to test the device in a simulated carotid artery containing an excised human plaque, in which blood flow is simulated by a flow of saline solution. By performing the angioplasty procedure in an environment which simulates conditions in human arteries, using an actual human plaque, emboli are produced under conditions which closely resemble those produced by dilation of the stenosis and implantation of a stent in a human patient.

11. One model that is used to determine whether an embolic filter device is effective to remove emboli from the bloodstream during carotid angioplasty procedures uses a surgically excised human carotid artery plaque, which is encased in a simulated artery made of PTFE (Teflon). Blood flow through the artery is simulated using saline solution, and emboli are released from the plaque during treatment procedures such as balloon catheter dilation of the stenosis and insertion of a stent. The embolic protection filter is examined following the procedure to determine whether emboli are successfully removed from blood flowing through the filter.

12. The use of this model has the additional, significant advantage that a downstream filter captures any emboli which are not removed by the deployed embolic filter. It is thus possible to establish that the filter successfully performs the function of

removing emboli, even though such proof would not be possible in human clinical trials. In a human clinical experiment, it would not be possible to quantify as accurately the amount of embolic particles either captured or released by the filter.

13. For these reasons, in my opinion, tests of an embolic filter protection device using a model which accurately simulates conditions in human carotid arteries, are reliable in determining whether a filter successfully removes released emboli from the bloodstream. Tests using an excised human plaque, and saline solution flowing through the simulated artery, permit more accurate determination of whether emboli of interest are removed from the simulated blood flow, than could be obtained by tests conducted using human or animal subjects. In my opinion, there is a high degree of correlation between successful tests of an embolic filter conducted using the above described test, and successful use of the embolic filter in actual carotid artery angioplasty/stenting procedures performed on human patients.

14. The test described herein also permits the success of an angioplasty/stenting procedure using the embolic filter to be evaluated by fluoroscopic and endoscopic observation.

15. Prior to March 5, 1998, Paul Gilson disclosed to me at a meeting at Dromoland Castle in Ireland, a stepped guidewire having a 0.013″/0.016″ design that achieved a "fail safe" interface between the guidewire and embolic filter. Exhibit 99 is a copy of a slide used by Paul Gilson during our meeting to describe the stepped guidewire and its "fail safe" interface with an embolic filter.

16. In January, 1998, Chas Taylor of MedNova contacted me to inquire whether I would perform tests of MedNova's prototype NeuroShield embolic filter protection device, using the test described herein.

17. On March 14, 1998, I tested the "NeuroShield" embolic filter at Montefiore Hospital in the Bronx, New York, USA. Exhibit 31 is a facsimile which I received from Chas Taylor on March 11, 1998, outlining an agenda for our meeting.

18. The filter element of prototype "Mark 1" NeuroShield filter device and system corresponding to one which I used in the March 14, 1998 tests is shown in Exhibit 90.

19. Fluoroscopic and angioscopic images recorded during the March 14, 1998 test were recorded, including images attached as Exhibit 91.

20. MedNova employees Paul Gilson and Chas Taylor attended the March 14, 1998 test.

21. The March 14, 1998 test was performed using simulated artery containing a surgically explanted human carotid artery plaque, which was sutured into a PTFE surgical graft to simulate an artery. Distal vasculature was represented by a 5 mm PTFE graft sutured to the system. The whole assembly was mounted in a water bath that was not temperature controlled, with access to the lesion by way of Teflon catheters. Endoscopic and fluoroscopic imaging was recorded. A filter was set up distally to capture any material not retained by the MedNova filter. Blood flow through the simulated artery and the embolic filter was simulated using saline solution flowing by gravity through the simulated artery. This test procedure is correctly described in a memorandum describing the tests prepared by Paul Gilson (Exhibit 37).

22. The "NeuroShield" device which I tested on March 14, 1998 utilized a stepped guidewire having a distal stop. The distal end of the guidewire had a diameter (*i.e.*, 0.016″) that was greater than the diameter of the polyimide tube filter support, and provided a stop which prevented distal translation of the filter element beyond the guidewire distal stop. The region of the guidewire proximal to the distal stop had a diameter (*i.e.*, 0.013″) that was smaller than the lumen of

the polyimide tube supporting the filter. It was therefore possible to rotate and translate the guidewire relative to the filter and its polyimide support.

23. In the "NeuroShield" device which I tested on March 14, 1998, the balloon filter element had a filter sac attached to a Nitinol framework having a number of self-expanding struts, and the Nitinol framework was attached to a thin polyimide filter support.

24. In the "NeuroShield" device, which I tested on March 14, 1998, the stepped guidewire was backloaded through the polyimide tube filter support. The distal end of the stepped guidewire would not pass through the polyimide tube filter support, and provided a distal stop on the guidewire. The filter element was thus disposed for translation on the guidewire proximal of the distal stop.

25. A version of the prototype embolic filter that I used in the March 14, 1998 tests, including a filter sac supported by self-expanding Nitinol struts, and the polyimide tube filter support, is accurately shown in Exhibit 90.

26. The balloon filter structure of the filter that was used in the March 14, 1998 tests is also schematically shown in Exhibit 65:

27. The structure of this filter is clearly visible in the fluoroscopic images, including the Nitinol struts which expand when the filter is released from the delivery catheter, and the platinum end marker, as shown in Exhibit 91 ("2:55 Nitinol filter frame deployed in vessel").

28. The expanded filter used in the March 14, 1998 tests is shown disposed on a mandrel in Exhibit 90. In order to transluminally insert the filter into the vessel, it was necessary to compress the filter using a loading device, and to insert the compressed filter and guidewire into a delivery catheter as shown in Exhibit 91 ("2:21 loaded filter and guidewire").

29. During the March 14, 1998 test, the guidewire and compressed filter element were first inserted into a delivery catheter.

30. A fluoroscopic image of the simulated vessel, containing a human plaque obstructing the vessel, is shown in Exhibit 91 ("2:39 plaque in vessel").

31. I transluminally inserted the delivery catheter, including the guidewire and compressed filter, into the simulated vessel.

32. I then successfully crossed the plaque narrowing the vessel with the guidewire, as shown in Exhibit 91 ("2:46 guidewire crosses lesion" and "2:50 steerable guidewire distal of lesion"). During this procedure, the guidewire was maneuvered through the lesion, and the guidewire rotated and translated distally with respect to the filter element, without displacing it.

33. The delivery catheter was used to transluminally insert the filter and guidewire to a position distal of the plaque in the vessel.

34. The filter was then deployed so that the struts and filter sac thereof expanded to engage a wall of the vessel, as shown in Exhibit 91("2:55 Nitinol filter frame deployed in vessel").

35. I then advanced a stent system (*i.e.*, a treatment device) along the guidewire to a position proximal to the location of the deployed filter, and retracted the sheath so that the stent was expanded over the lesion, as shown in Exhibit 91 ("3:28 expanded stent, stent cathether and filter").

36. Emboli were released when the plaque was dislodged by the stent.

37. I then retracted the stent catheter, and injected contrast agent.

38. The expanded stent and the distal end marker of the embolic filter are shown in Exhibit 91 ("3:50 expanded stent and filter marker"). Injected contrast agent shows the opened vessel, stent and filter device, in Exhibit 91("3:57 flow through stent and filter").

39. I advanced a balloon catheter along the Guidewire to a position over the plaque. I then expanded the balloon over the stent and lesion.

40. The expansion of the balloon released further emboli from the plaque.

41. I then advanced a retrieval catheter along the guidewire to the distal end of the stent and proximal of the expanded filter, as shown in Exhibit 91("4:00 retrieval catheter pod in angioplastied stent and lesion").

42. I then retracted the guide wire in a proximal direction to cause the distal stop of the guidewire to abut against the polyimide filter support.

43. While holding the retrieval catheter in position, I retracted the filter into the retrieval catheter to collapse the filter, as shown in Exhibit 91("4:05 retracting filter into retrieval catheter pod" and "4:09 filter retracted into retrieval catheter"). I then removed the retrieval catheter containing the filter from the vessel.

44. I then removed the filter from the retrieval catheter and it was cut open. A number of large embolic particles were visible in the opened filter.

45. These tests confirmed that the filter filtered emboli out of the saline solution flowing through the simulated artery.

46. During the simulated treatment procedure described in paragraphs 34-41, I found that the system successfully crossed the lesion, deployed the filter, captured embolic material and was retrieved.

47. During the procedure described in paragraphs 30-41, the guidewire was rotated and translated relative to the filter element, both before deployment and after expanding the filter in the vessel. I found that rotation and translation of the guidewire relative to the filter element did not displace the expanded filter element deployed in the vessel. Rotation and translation of the guidewire prior to deployment did not displace the compressed filter element in the delivery catheter.

48. During the procedure described in paragraphs 30-41, I found that rotation or distal translation of the guide wire was possible, although manipulation of the guidewire at times was difficult due to friction between the guidewire and the polyimide support of the filter.

49. During the procedure described in paragraph 33, I found that, although the filter element deployed in the vessel so that the struts and filter sac expanded to engage a wall of the simulated artery, the filter sac creased during deployment, and did not completely close the vessel.

50. The results of the March 14, 1998 tests are accurately described in Paul Gilson's March 18, 1998 memorandum, attached as Exhibit 37.

51. Paul Gilson's March 18, 1998 memorandum correctly states that the 0.013″/0.016″ stepped guidewire was used in the March 14, 1998 test, with a 6mm NeuroShield filter, and that the guidewire moved distally/proximally in the filter shaft.

52. After the March 14, 1998 test, it is my understanding that the inventors designed a subsequent version of the "NeuroShield" embolic filter which provided a filter element intended to provide better movement of the guidewire.

53. On March 24, 1998, Paul Gilson disclosed the revised version of the "NeuroShield" embolic filter to me in a facsimile (Exhibit 60).

54. In his March 24, 1998 facsimile, Paul Gilson described MedNova's changes to the "NeuroShield" embolic filter utilized in the March 14, 1998 test, which included mounting the filter on a short polyimide tube support to which the Nitinol filter support was bonded. This configuration allowed the filter assembly to freely move between pre-determined stops on the guide wire, and thus the wire was free to torque and to have limited movement longitudinally (Exhibit 60, page 3).

55. In his March 24, 1998 facsimile, Paul Gilson also informed me that MedNova would be ready by April 3rd or 4th, 1998, to evaluate the revised "NeuroShield" embolic filter (Exhibit 60, page 1).

56. On April 5, 1998, I tested the revised version of the "NeuroShield" embolic filter at Montefiore Hospital in the Bronx, New York, USA. (Exhibits 79, 81).

57. Paul Gilson and Chas Taylor attended the April 5, 1998 test.

58. The April 5, 1998 test was performed using the simulated artery described above.

59. The "NeuroShield" device tested on April 5, 1998 utilized a stepped (0.013″/0.016″) guidewire having an improved distal stop.

60. In the revised "NeuroShield" device, the stepped guidewire was preloaded through a balloon filter element having a filter sac which was affixed to a Nitinol support having a number of self-expanding struts.

61. In the revised "NeuroShield" device, the Nitinol structure was attached to a short (about 40 mm) polyimide tube support disposed, between the distal stop and a proximal stop, as shown in Exhibit 60, page 3, and Exhibits 81 and 88). Because the short polyimide tube had a lumen with an inner diameter smaller than the diameter of the distal stop of the guidewire, the distal stop of the guidewire would not pass through the polyimide tube and provided a distal stop. The filter element was disposed for translation and rotation on the stepped guidewire proximal of the distal stop.

62. The short polyimide tube (about 40 mm) floated on the guidewire between the distal stop and the proximal stop. The filter element was thus capable of rotation and distal translation with respect to the guidewire in a manner equivalent to the earlier version of the device.

63. The modified NeuroShield filter and guidewire which I tested on April 5, 1998, are accurately described in Exhibit 88

64. During the April 5, 1998 test, I first inserted the guidewire and compressed filter element into a delivery catheter.

65. I then transluminally inserted the delivery catheter, including the guidewire and compressed filter, into the simulated vessel.

66. I then successfully crossed the plaque narrowing the vessel with the delivery catheter, to a position distal of the plaque.

67. I then deployed the filter element so that the struts and filter sac thereof expanded to engage a wall of the vessel.

68. I then advanced a balloon dilation catheter (*i.e.*, a treatment device) along the guidewire to a position proximal to the location of the deployed filter, and expanded the balloon to dilate the plaque (*i.e.*, treat a portion of the vessel) so that the lesion was angioplastied.

69. I then retracted the balloon catheter, and advanced a stent along the guidewire to a position over the plaque, where the stent was expanded.

70. During the above steps, emboli were dislodged from the plaque, and were successfully captured in the filter.

71. I then advanced a retrieval catheter along the guidewire to a position distal of the stent and proximal of the expanded filter.

72. I then retracted the guide wire in a proximal direction to cause the distal stop of the guidewire to abut against the polyimide filter support.

73. I then pulled the filter into the pod of the retrieval catheter, and removed the retrieval catheter containing the filter from the simulated artery.

74. I then removed the filter from the retrieval catheter and cut it open. A number of large embolic particles were visible in the opened filter.

75. I thus confirmed that the filter filtered emboli out of the saline solution flowing through the simulated artery.

76. During the procedure described in paragraphs 67-71, I found that the system successfully crossed the lesion, deployed the filter, captured embolic material and was retrieved.

77. During the procedure described in paragraphs 64-71, rotation and distal translation of the guide wire relative to the deployed filter was maintained and improved in comparison with the "NeuroShield" device which I tested on March 14, 1998.

78. During the procedure described in paragraphs 64-71, the guidewire was rotated and translated relative to the filter element, both before deployment and after expanding the filter in the vessel. I found that rotation and translation of the

guidewire relative to the filter element did not displace the expanded filter element deployed in the vessel. Rotation and translation of the guidewire prior to deployment did not displace the compressed filter element in the delivery catheter.

79. During the procedure described in paragraphs 64-71, movement and interface, as well as handling of the filter during both preparation and use, were maintained and improved in comparison with the "NeuroShield" device which I tested on March 14, 1998.

80. Based on my experience in endovascular surgery, the tests of the NeuroShield filter which I performed on March 14, 1998 and April 5, 1998, demonstrated that the system successfully crossed the lesion, deployed the filter, captured embolic material and was retrieved, and that the system would successfully perform the function of removing emboli from blood flowing through a vessel during carotid artery angioplasty procedures in a human patient. In my opinion, the test results of the modified NeuroShield filter which I performed on March 14, 1998 and April 5, 1998, are sufficiently correlated with the conditions found in actual angioplasty procedures on human patients, to establish that the NeuroShield embolic filter would perform its intended function of filtering emboli from the blood of a patient undergoing carotid angioplasty procedures, in a human artery. For the reasons I have noted above, the simulated test is in some respects more reliable than *in vivo* tests in a human patient. I consider that the tests which I conducted on March 14, 1998 and April 5, 1998 established the practical utility of the embolic filter device for use in carotid angioplasty procedures. I am not aware of any other test, including human clinical trials, that would be more probative of the successful function of the embolic filter protection device and system developed by MedNova.

I declare that all the statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: 1/4/06

Dr. Gary Roubin